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REMARKS

Examination and prompt and favorable consideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.115, are respectfully requested.

This Preliminary Reply and accompanying arguments address the rejections maintained in the Final Official Action dated August 15, 2001.

As correctly indicated in the Office Action Summary, claims 15 and 16 were pending in this application when last examined. Therefore, claims 15 and 16 are currently pending.

I. THE 35 U.S.C. § 101 AND § 112, FIRST PARAGRAPH, REJECTIONS

Claims 15 and 16 have been rejected under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, as allegedly lacking either a credible asserted utility or a well established utility, and that as a result, one skilled in the art would not know how to use the claimed invention. August 15, 2001, Office Action, page 2. Applicants respectfully traverse these rejections.

a. THE SPECIFICATION ASSERTS A CREDIBLE UTILITY FOR THE CLAIMED INVENTION

To satisfy the utility requirement under 35 U.S.C. § 101, the claims and the specification must disclose either a credible "well-established utility" or a credible "asserted utility" for the claimed invention. See M.P.E.P. § 2107.01; see also Brenner v. Manson, 383 U.S. 519, 148 U.S.P.Q. 689 (1966). It is well established that a "specific asserted utility" is an explicit statement of "why the applicant believes that the invention is

useful." See M.P.E.P. § 2107.02. Such statements will usually explain the purpose of how the invention may be used. Id. Section 2107.02 of the Manual of Patent Examing Procedure ("M.P.E.P.") also states that utility under 35 U.S.C. § 101 is met, even if a specific, substantial and credible utility for the claimed invention is not asserted in the specification, if such utility is well-established. The M.P.E.P., in section 2107.02, further defines an invention having a well-established utility as any invention where:

> (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible. If an invention has a well-established utility, rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, based on lack of utility should not be imposed.

Id. Thus, a well-established utility is well known, immediately apparent and/or implied by the specification based on the disclosure of the properties of the claimed invention, either alone or taken with knowledge of one skilled in the art.

Moreover, it is well settled that the threshold of utility is not high: ***An invention is "useful" under § 101 if it is capable of providing some identifiable benefit.*** See, Juicy Whip, Inc. v. Orange Bang, 51 U.S.P.Q.2d 1700 (citing Brenner, 383 U.S. at 534); see also Brooktree Corp. v. Advanced Micro Devices, Inc., 977 F.2d 1555, 1571 (Fed. Cir. 1992) ("To violate § 101 the claimed device must be totally incapable of achieving a useful result"); Fuller v. Bergg, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is incapable of serving any beneficial end . . ."). Applicants further note that the Federal Register, Vol. 66, No. 4, 1097 (2001) also states:

> ***Only one*** specific, substantial, and credible utility is required to satisfy the statutory requirement. Where one or more well-established utilities would have been readily apparent to those of skill in the art at the time of the invention, ***an applicant may rely on any one of those utilities*** without prejudice. (Emphasis added).

Thus, the case law indicates that only one credible specific or well-established utility is required and that the threshold for satisfying utility is not high.

Applicants submit that the Specification of the present application satisfies these utility requirements. For instance, the claimed invention is directed to a method for detecting and/or quantifying a nucleic acid coding for the SMR1 polypeptide. In this regard, the Specification discloses methods for analyzing the accumulation of mRNA encoding for the SMR1 polypeptide in the SMG of the rat. See, e.g., Specification, page 11, line 20 to page 12, line 34. In particular, the Specification teaches that androgen treatment leads to a high degree of accumulation of mRNA coding for the SMR1 polypeptide in the SMG of the rat. See, e.g., Specification, page 1, lines 28-30, page 12, lines 29-30. The Specification further teaches that the nucleic acids of the present invention encode the SMR1 polypeptide which gives maturation products with physiological activity. See, e.g., Specification, page 1, lines 27-30. Based on this disclosure, one of skill in the art would find it credible that the claimed invention has utility as a diagnostic to assess the level of androgen activity.

As explained in the Declaration under 37 C.F.R. § 1.132 by Dr. Rosinski-Chupin ("Rosinski-Chupin Declaration") submitted along with the Amendment and Reply of May 29, 2001, the disclosure of the subject application teaches the high degree of induction of the SMR1 gene by androgens. See, e.g., Specification, page 12, lines 20-30. The

Rosinski-Chupin Declaration explains that the involvement of the SMR1 polypeptide in biological responses regulated by androgens makes it possible to use nucleotide probes to detect SMR1 encoding nucleic acids in order to evaluate androgen activity. Rosinski-Chupin Declaration, page 2, 3rd paragraph. Accordingly, the accumulation of mRNA coding for SMR1 is correlatable to androgen activity, and thus useful as a diagnostic of androgen activity or anti-androgen activity of new drugs. Similarly, assessing the level of nucleic acids encoding SMR1 is useful to reveal abnormalities in androgen activity. Thus, the claimed invention is useful as a diagnostic to assess androgen activity.

As further support that assessing the level of nucleic acids encoding SMR1 is useful as a diagnostic marker of androgen activity (or anti-androgen activity) of new drugs, Applicants submit that the following references (copies of which have been attached hereto): John Trachtenberg, THE JOURNAL OF UROLOGY, Vol. 132: 61-63 (1984) ("Trachtenberg"); Lacoste et al., J. STEROID BIOCHEMISTRY, Vol. 31, No. 6: 963-970 (1988) ("Lacoste"); Lambert et al., J. ENDOCR., Vol. 113: 457-461 (1987); Furr, EUROPEAN UROLOGY, Suppl. 2: 83-95 (1996) ("Lambert"), Muntzing et al., INVESTIGATIVE UROLOGY, Vol. 17, No. 3: 176-180 (1979) ("Muntzing"); and DeLellis et al., THE JOURNAL OF HISTOCHEMISTRY AND CYTOCHEMISTRY, Vol. 35, No. 11: 1347-1351 (1987) ("DeLellis").

Trachtenberg demonstrates that the nonestrogenic antifungal agent, ketonazole, has an anti-androgen effect and that this drug may prove to be a new prostatic cancer agent. In particular, the last sentence of the Abstract on page 61 indicates that the anticancer drug, ketonazole, results in a decrease in testicular androgen levels.

Similarly, Lacoste discloses that the administration of anti-cancer agents, such as ketonazole and aminoglutethimide, result in decreases of testicular androgen. Moreover, Lacoste at page 969, last sentence suggests adding an antiandrogen to the inhibitors of steroid biosynthesis in order to achieve a more complete blockage of androgen activity, thereby suppressing the growth of androgen-sensitive tumors. Based on these references and the teachings in the Specification, one of skill in the art would readily appreciate that certain drugs affect the level of androgen activity. Accordingly, these references clearly demonstrate the importance of assessing the level of androgen in the development of new drugs.

Lambert assesses the effect of drugs affecting testicular steroidgenesis on mouse cells. Preparations of Leydig cells (*i.e.*, endocrine cells) were used. The inhibition of testosterone secretion was measured. Lambert indicates that simple assay methods, such as *in vitro* tests utilizing mouse cells, have application in pharmacology and the development of new drugs.

The Muntzing article discusses the effect of the anticancer agent, Tadenan, on testosterone levels in the rat. In particular, Muntzing demonstrates that the assessment of RNA and DNA concentrations is useful as an indicator of drug activity. Muntzing, page 178, 2nd column, 1st paragraph.

The Furr article discloses the use of rat and mouse cell *in vitro* studies to assess the effect of the anticancer drug, Casodex, in the preclinical setting. Furr also indicates that Casodex is an antiandrogen that binds to rat, dog, and human prostrate androgen receptors

transfected into COS-1 cells. See, e.g., Furr, Abstract; page 86, 1st column, last sentence, to 2nd column, 1st sentence.

The DeLellis review article provides evidence that hybridization techniques for measuring DNA or RNA encoding regulatory proteins serve as important diagnostic tools for the assessment of various disorders. In particular, this review article explains that the analysis of gene expression at the levels of mRNA and genomic DNA provides an important approach for the diagnostic and prognostic assessment of disorders of the endocrine system. See, e.g., DeLellis, Abstract, and page 1347, 2nd column, second paragraph.

Therefore, in view of the above teachings and the Specification's disclosure, one of skill in the art would readily appreciate that the claimed invention has utility as a diagnostic indicator to assess androgen activity in the development of new drugs.

b. THE CLAIMED INVENTION HAS A SUBSTANTIAL UTILITY

"Substantial utility" is defined in the Training Materials of the United States Patent and Trademark Office as "a utility that defines a "real world" use. For example, . . . an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use." Revised Interim Utility Guidelines Training Materials of the United States Patent and Trademark Office, at page 6.

Applicants submit that the development of diagnostic assays to assess the level of androgen activity is a "real world" utility and that these utilities are in concordance with the printed policies espoused by the United States Patent and Trademark Office. Certainly, based on the Utility Examination Guidelines, such a use cannot and would not be

categorized by the skilled artisan nor the Office as "'throw away,' 'insubstantial,' or 'nonspecific' utilities, such as the use of a complex invention as landfill, as a way of satisfying the utility requirement of 35 U.S.C. 101." 66 Fed. Reg. 1098 (2001). Applicants submit that credible utility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record. See Utility Examination Guidelines, 66 Fed. Reg. 1092 (2001). Moreover, the Training Materials describe how this standard is to be applied:

> Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion.

Revised Interim Utility Guidelines Training Materials, at page 5, (http://www.uspto.gov/web/offices/pac/utility/utilityguide.pdf). Applicants submit that the use of polynucleotides in diagnostic assays is well known in the art and, thus, would not be seriously flawed or be based on inconsistent logic. Additionally, the utilities posited by Applicants are not "landfill throw-aways." Thus, the skilled artisan, upon reading the disclosure and with the knowledge of the art would have no reason to doubt that the claimed invention could be used for these purposes.

Applicants further direct the Examiner's attention to M.P.E.P. § 2107.01 (I) which recognizes that "[m]any research tools . . . have a clear, specific, and unquestionable utility (e.g., they are useful in analyzing compounds)." This clearly indicates that many research tools are useful in a patent sense. Therefore, polynucleotides which can be used

to assess the accumulation of mRNA coding for SMR1 meet the utility requirement of 35 U.S.C. § 101.

Thus, as previously asserted, Applicants invention is certainly ***not*** landfill throwaway and easily would be appreciated by the skilled artisan as a research tool. To construe that research tools do not possess utility or that such a utility is insufficient to meet the Examiner's interpretation of the Utility Examination Guidelines is in direct contravention of the guidance set forth by the M.P.E.P., the Utility Examination Guidelines and the Courts. Applicants respectfully submit that for ***at least*** these reasons, the claimed invention is entitled to patent protection.

c THE OFFICIAL ACTION FAILS TO SET FORTH A *PRIMA FACIE* SHOWING OF LACK OF UTILITY UNDER 35 U.S.C. § 101

With regard to patentable utility, the M.P.E.P. states at § 706.03(a)(1), that a *prima facie* showing must containing the following:

(i) a well-reasoned statement that clearly sets forth the reasoning used in concluding that the asserted utility is not credible;
(ii) support for factual findings relied upon in reaching this conclusion; and
(iii) support for any conclusions regarding evidence provided by the applicant in support of an asserted utility.

Moreover, it is well established that an asserted utility is presumed true. See M.P.E.P. § 2107.01; In re Brana, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). To overcome the presumption that a specific utility is lacking, the Office must show by a ***preponderance of evidence*** that it is ***more likely than not*** that the asserted utility would be considered false by a person of ordinary skill. See M.P.E.P. § 2107.01; In re Corkill, 226 U.S.P.Q. 1005, 1008 (Fed. Cir. 1985). Further, the Federal Circuit has reinforced that to

sustain a rejection under 35 U.S.C. § 101, the claimed invention "must be ***totally incapable of achieving a useful result***." Brooktree Corp. v. Advanced Micro Devices, Inc., 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992) (emphasis added); see also, E.I. du Pont de Nemours & Co. v. Berkley and Co., 620 F.2d 1247, 1260 n.17, 205 U.S.P.Q. 1, 10 n.17 (8th Cir. 1980). Additionally, Applicants assert that the Office "cannot make this type of rejection, however, unless it has reason to doubt the objective truth of the statements contained in the written description." In re Cortright, 49 U.S.P.Q.2d 1464, 1466 (Fed. Cir. 1999) (citing In re Brana, 51 F.3d 1160, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995)). "The PTO may establish a reason to doubt an invention's asserted utility when the written description suggest[s] an ***inherently unbelievable*** undertaking or involve[s] ***implausible scientific principles***." Cortright, 49 U.S.P.Q. at 1466 (citing Brana 51 F.3d at 1566, 34 U.S.P.Q.2d at 1441 (emphasis added)). Applicants assert that the claimed invention is neither inherently unbelievable nor involves an implausible scientific principle. Applicants further submit that ***only one*** credible assertion of specific and substantial utility for the claimed invention is necessary to satisfy the utility requirement. M.P.E.P. § 2107. Moreover, as indicated above, the ***threshold of utility is not high***. See Brenner, 383 U.S. at 534.

Applicants respectfully submit that the Examiner has not met this burden for lack of utility under 35 U.S.C. § 101 and for how to use under 35 U.S.C. § 112, first paragraph. The Examiner appears to base the instant rejection on an allegation that it is not clear that subjecting rats to new drugs and the subsequent measurement of the claimed polynucleotides is indicative of modulation of androgen levels. However, the Examiner

fails to provide evidence that the biological function is other than posited. The Examiner further argues that Applicants have not provided objective evidence to support the claimed hybridization methods as a pharmaceutical screening tool. August 15, 2001, Office Action, page 2. However, the Specification at page 11, line 20 to page 12, line 18 teaches the assessment of the regulation of the accumulation of mRNA which encodes the SMR1 polypeptide in the SMG of the rat by androgen treatment. Moreover, Applicants submit that the references discussed above satisfy the Examiner's request for evidence that the measurement of androgen levels at a preclinical stage, particularly, in rats or mice, is important for new drug development.

Accordingly, absent evidence that directly refutes the utility posited in the application, Applicant submits that the utility is credible, and the presumptive truth of the utility should not be doubted. Thus, the withdrawal of the rejections under 35 U.S.C. §§ 101 and 112, first paragraph, is respectfully requested.

II. THE 35 U.S.C.§ 112, SECOND PARAGRAPH, REJECTION

Claims 15 and 16 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the claimed invention. August 15, 2001, Office Action, page 2. The Examiner believes that without a recitation as to the level of stringency, the term "hybridize" encompasses many different levels of stringency, leading to many different experimental outcomes. Applicants respectfully traverse this rejection.

Applicants assert that the "hybridization" of a probe to nucleic acid is well within the purview of those skilled in the art as demonstrated in the DeLellis review article discussed above. This reference teaches that hybridization techniques for measuring DNA or RNA encoding regulatory proteins serve as important diagnostic tools for the assessment of various disorders. Further, the Specification clearly provides hybridization conditions for hybridizing a probe to RNA. See, e.g., Specification, page 8, lines 20-32. Therefore, one of skill in the art would readily understand what is meant by the term "hybridize."

Finally, Applicants assert that the claims require that any detected nucleic acid must still encode for the SMR1 polypeptide. Thus, contrary to the Examiner's position the claimed invention will not lead to many different experimental outcomes, but only those nucleic acids that encode the SMR1 polypeptide.

Accordingly, Applicants respectfully request the withdrawal of this rejection.

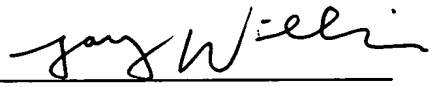
CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: 

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Attachment to Preliminary Amendment (4 References)